

**Amendments to the Abstract**

Please replace the paragraph at page 119, lines 1 through 12 with the following amended paragraph:

**METHODS FOR IDENTIFYING AGENTS THAT ALTER NAD-DEPENDENT  
DEACETYLATION ACTIVITY OF A SIR2 PROTEIN WHICH ALTER HISTONE PROTEIN  
ACETYLATION, DECREASE AGING OR INCREASE LIFESPAN**

Methods of identifying agents which alter the NAD-dependent deacetylation activity of a Sir2 protein or a fragment of a Sir2 protein acetylation-status and mono-ADP-ribosylation of nuclear proteins are disclosed. The acetylated protein can be a nuclear protein, such as a histone protein, or a cytoplasmic protein. The Sir2 protein employed in the methods can include at least a core domain of a Sir2 protein, such as a human Sir2 protein. The methods further include identifying agents which alter the life span or aging of a cell or an organism by determining the level of NAD-dependent acetylation and/or ADP-ribosylation of a nuclear protein. The invention also relates to a mammalian Sir2 protein which acetylates or deacetylates nuclear proteins in a NAD-dependent manner and has mono-ADP-ribosyltransferase activity. Host cells producing the Sir2 protein and antibodies to the Sir2 protein are also provided.